10/613/06

5 search results

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Term: (E1b or E1b) near5 ("same" or identical or different or heterologous) near5 promoter$

Display: 100 **Documents in Display Format:** - **Starting with Number** 1

Generate: ○ **Hit List** ◉ **Hit Count** ○ **Side by Side** ○ **Image**

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Search History

DATE: Friday, March 11, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L7	L3 and retrovir$ near5 vector$	6	L7
L6	L5 and retrovir$ near3 vector$	2	L6
L5	l3 and (A549 or PC-3)	11	L5
L4	l3 and A549	11	L4
L3	(E1b or E1b) near5 ("same" or identical or different or heterologous) near5 promoter$	22	L3
L2	(E1a or E1b) near5 ("same" or identical) near5 promoter$	16	L2
L1	(E1b or E1b) near5 ("same" or identical) near5 promoter$	10	L1

END OF SEARCH HISTORY

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Term: "pIG.E1A.E1b"

Display: 100 **Documents in Display Format:** - **Starting with Number** 1

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Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L5	"pIG.E1A.E1b"	27	L5
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=OR			
L4	per.c6 near10 e1b	19	L4
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L3	Per.c6 near10 promoter$ near5 (E1a or E1b)	4	L3
L2	cell near3 line$ near10 (E1a or E1b) near5 promoter$ near5 heterologous	4	L2
L1	(E1a or E1b) near5 promoter$ near5 heterologous	43	L1

END OF SEARCH HISTORY

Freeform Search

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Term:

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Generate: ○ **Hit List** ◉ **Hit Count** ○ **Side by Side** ○ **Image**

Search Clear Interrupt

Search History

DATE: Sunday, March 13, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L9	l4 and integrat$ near5 (multipl$ or different$)	10	L9
L8	L6 and integrat$	2	L8
L7	L6 and a549	1	L7
L6	20010049136	2	L6
L5	cell$ near10 (E1a or E1b) near5 (regulat$ or induci$) near5 promoter$	39	L5
L4	(E1a or E1b) near5 (regulat$ or induci$) near5 promoter$	125	L4
L3	(E1a or E1b) near5 (regulat$ or induci$) near5 promoter4	0	L3
L2	phosphoglycerate near kinase near5 inducib$	94	L2
L1	phosphoglycerate near kinase near5 regulat$	66	L1

END OF SEARCH HISTORY

Freeform Search

Database: US Pre-Grant Publication Full-Text Database
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Term: L16 and a549 and integrat$

Display: 100 **Documents in Display Format:** - **Starting with Number** 1

Generate: ○ **Hit List** ◉ **Hit Count** ○ **Side by Side** ○ **Image**

Search Clear Interrupt

Search History

DATE: Sunday, March 13, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L27	cell$ near10 (E1a or E1b) near5 promoter$ near5 RSV	10	L27
L26	(E1a or E1b) near5 promoter$ near5 RSV	110	L26
L25	(E1a or E1b) near5 promoter$ near5 retrovir$	18	L25
L24	L23 and substantially	1	L24
L23	20050003545	2	L23
L22	L14 and (inducib$ or regulatab$)	1	L22
L21	L14 and (E1a or E1b) near5 promoter$ and producer near5 cell$	0	L21
L20	L14 and (E1a or E1b) near5 promoter$ and packaging near5 cell$	0	L20
L19	L14 and (E1a or E1b) near5 promoter$	1	L19
DB=PGPB,USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L18	l14 and constitutiv$	1	L18
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L17	L16 and a549 and integrat$	1	L17
L16	6040174 [pn]	2	L16
L15	L14 and integrat$	2	L15

L14	20010049136	2	L14
L13	PER.C6 and integrat$ near10 (multiple$ or different$ or tandem$)	35	L13
L12	PER.C6 near10 integrat$ and integrat$ near10 (multiple$ or different$ or tandem$)	3	L12
L11	PER.C6 near10 integrat$ near10 (multiple$ or different$ or tandem$)	0	L11
L10	PER.C6 near10 integrat$ near10 (multiple$ or different$)	0	L10
L9	PER.C6 near5 integrat$ near5 (multiple$ or different$)	0	L9
L8	PER.C6 near5 integrat$	16	L8
L7	PER.C6 and integat$	0	L7
L6	PER.C6 and intergat$	0	L6
L5	PER.C6	146	L5
L4	PER.C6 near25 integat$	0	L4
L3	PER.C6 near15 integat$	0	L3
L2	PER.C6 near5 integat$	0	L2
L1	PER.C6 near5 intergat$	0	L1

END OF SEARCH HISTORY

Your wildcard search against 10000 terms has yielded the results below.
Your result set for the last L# is incomplete.
The probable cause is use of unlimited truncation. Revise your search strategy to use limited truncation.

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Search Results - Record(s) 1 through 39 of 39 returned.

1. 20050019829. 30 Dec 03. 27 Jan 05. Protein/solubility folding assessed by structural complementation. Thomas, Philip Jordan, et al. 435/7.1; 435/455 G01N033/53 C12N015/85.

2. 20050003545. 03 Jul 03. 06 Jan 05. Adenovirus packaging cell lines. Li, Yuanhao, et al. 435/456; 435/325 435/366 C12N005/08 C12N015/861.

3. 20050003506. 28 May 04. 06 Jan 05. Adenoviral E1A/E1B complementing cell line. Li, Yuanhao, et al. 435/235.1; 435/366 C12N007/00 C12N005/08.

4. 20050002905. 12 Apr 04. 06 Jan 05. RAAV vector-based pro-opiomelanocortin compositions and methods of use. Scarpace, Philip J., et al. 424/93.2; 435/456 A61K048/00 C12N015/861.

5. 20040126846. 24 Sep 03. 01 Jul 04. Endogenous granzyme B in non-immune cells. Xu, Hong-Ji, et al. 435/69.1; 435/226 435/320.1 435/325 536/23.2 C12N009/64 C07H021/04.

6. 20040115198. 27 Aug 03. 17 Jun 04. Activation of lymphocyte populations expressing NKG2D using anti-NKG2D antibodies and ligand derivatives. Spies, Thomas, et al. 424/145.1; A61K039/395.

7. 20040086920. 20 Aug 03. 06 May 04. STARS - a muscle-specific actin-binding protein. Olson, Eric, et al. 435/6; 435/320.1 435/325 435/69.1 530/350 536/23.5 C12Q001/68 G01N033/53 C07H021/04 C07K014/47.

8. 20040029158. 16 May 03. 12 Feb 04. HOP - a novel cardiac-restricted transcriptional factor potentially useful for cardiac regeneration and specification. Olson, Eric, et al. 435/6; 435/199 435/320.1 435/325 435/69.1 530/358 530/388.26 536/23.2 C12Q001/68 C07H021/04 C12N009/22 C12P021/02 C12N005/06 C07K016/40.

9. 20040009588. 24 Jun 03. 15 Jan 04. Vectors for tissue-specific replication and gene expression. Chang, Yung-Nien, et al. 435/320.1; 514/44 A61K048/00 C12N015/00.

10. 20040002065. 31 Jan 01. 01 Jan 04. PROTEIN/SOLUBILITY FOLDING ASSESSED BY STRUCTURAL COMPLEMENTATION. Thomas, Philip Jordan, et al. 435/6; 435/7.1 C12Q001/68 G01N033/53.

11. 20030152914. 31 May 02. 14 Aug 03. Method for generating replication defective viral vectors that are helper free. Kaplitt, Michael G., et al. 435/5; 435/235.1 435/320.1 435/456 435/6 C12Q001/70 C12Q001/68 C12N007/00 C12N015/861.

12. 20030138954. 02 Dec 02. 24 Jul 03. Methods and compositions relating to restricted expression lentiviral vectors and their applications. Trono, Didier, et al. 435/456; 435/235.1 435/320.1 C12N015/867 C12N007/00.

☐ 13. 20030109472. 30 May 02. 12 Jun 03. Replicating adenovirus vectors. Amalfitano, Andrea, et al. 514/44; 424/93.2 435/235.1 435/320.1 435/456 A61K048/00 C12N007/00 C12N015/861.

☐ 14. 20030108920. 09 Sep 02. 12 Jun 03. Tumor suppressor-like proteins that bind IGFBP2. Zhang, Wei, et al. 435/6; 435/320.1 435/325 435/69.1 435/7.23 514/12 514/44 530/350 536/23.2 800/18 A61K048/00 A61K038/17 A01K067/027 C12Q001/68 G01N033/574 C12P021/02 C12N005/06 C07K014/47.

☐ 15. 20030104625. 22 Feb 02. 05 Jun 03. Novel oncolytic adenoviral vectors. Cheng, Cheng, et al. 435/456; 435/199 435/235.1 435/320.1 C12N015/861 C12N009/22 C12N007/00.

☐ 16. 20030087247. 12 Feb 02. 08 May 03. Diagnosis and treatment of inflammation and hyperactive immune conditions. Kumamoto, Tadashi, et al. 435/6; 435/4 C12Q001/68 C12Q001/00.

☐ 17. 20030082789. 01 Aug 02. 01 May 03. Methods and compositions relating to improved lentiviral vector production systems. Trono, Didier, et al. 435/235.1; 435/366 435/456 C12N007/00 C12N005/08 C12N015/867.

☐ 18. 20030039657. 14 Apr 00. 27 Feb 03. Inducible vaccines. Johnston, Stephen Albert, et al. 424/184.1; 424/93.21 A61K048/00 A61K039/00.

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☐ 20. 20030008374. 09 Nov 01. 09 Jan 03. Methods and compositions relating to improved lentiviral vectors and their applications. Trono, Didier, et al. 435/235.1; 435/320.1 435/456 C12N015/867 C12N007/01.

☐ 21. 20020155432. 28 Nov 01. 24 Oct 02. Genetically engineered herpes virus for the treatment of cardiovascular disease. Schwartz, Lewis B., et al. 435/5; 424/199.1 424/205.1 424/229.1 435/320.1 435/69.1 C12Q001/70 C12P021/06 A61K039/12 A61K039/245 A61K039/255 A61K039/265 A61K039/27 C12N015/00 C12N015/09 C12N015/63 C12N015/70 C12N015/74.

☐ 22. 20020150953. 13 Feb 01. 17 Oct 02. Methods and compositions relating to muscle selective calcineurin interacting protein (MCIP). Williams, R. Sanders, et al. 435/7.23; 424/9.2 435/7.92 G01N033/574 G01N033/53 G01N033/537 G01N033/543 A61K049/00.

☐ 23. 20020137706. 20 Jul 01. 26 Sep 02. Regulated growth factor delivery for engineered peripheral nerve. Evans, Gregory R.D., et al. 514/44; 424/93.21 A61K048/00.

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☐ 25. 20020052485. 20 Apr 01. 02 May 02. Polynucleotides for use in recombinant adeno-associated virus virion production. Colosi, Peter. 536/23.1; 435/235.1 C07H021/02 C07H021/04 C12N007/00.

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☐ 28. 6676935. 10 Sep 98; 13 Jan 04. Tissue specific adenoviral vectors. Henderson; Daniel R., et al. 424/93.2; 424/93.6 435/320.1 435/325 435/456 514/44. A61K048/00 C12N005/00 C12N015/00.

☐ 29. 6638762. 19 Nov 97; 28 Oct 03. Tissue-vectors specific replication and gene expression. Chang; Yung-Nien, et al. 435/325; 424/93.2 435/320.1 435/455 435/69.1 435/91.4 514/44. C12N015/00 C12N015/63.

☐ 30. 6585968. 02 Jul 01; 01 Jul 03. Adenovirus vectors specific for cells expressing alpha-fetoprotein and methods of use thereof. Little; Andrew S., et al. 424/93.2; 424/93.1 424/93.6 435/320.1 435/325 435/366 435/455 435/456 435/457 435/69.1 536/23.1 536/24.1. A61K048/00 C12N015/861 C12N005/10 C12N015/63 C12N015/64.

☐ 31. 6495130. 29 Dec 99; 17 Dec 02. Target cell-specific adenoviral vectors containing E3 and methods of use thereof. Henderson; Daniel R., et al. 424/93.2; 424/93.1 424/93.6 435/320.1 435/325 435/455 514/44. A61K353/00 A61K048/00 C12N015/63 C12N015/85 C12N015/09.

☐ 32. 6436394. 11 Jul 00; 20 Aug 02. Adenovirus vectors specific for cells expressing androgen receptor and methods of use thereof. Henderson; Daniel R., et al. 424/93.2; 424/93.1 424/93.6 435/320.1 435/325 435/366 435/369 435/371 435/455 435/456 435/457. A61K048/00 C12N015/861 C12N005/10 C12N015/63.

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☐ 36. 5885829. 28 May 97; 23 Mar 99. Engineering oral tissues. Mooney; David J., et al. 435/325; 424/422 424/435 424/49 435/374 435/378 435/69.1. C12N005/00 C12N005/02 C12N005/08 C12N015/09.

☐ 37. 5871726. 26 Jun 96; 16 Feb 99. Tissue specific and tumor growth supperssion by adenovirus comprising prostate specific antigen. Henderson; Daniel Robert, et al. 424/93.2; 424/93.6 435/320.1 435/325 435/456. A61K048/00 C12N005/00 C12N015/00.

☐ 38. 5474935. 03 Nov 93; 12 Dec 95. Adeno-associated virus (AAV)-based eucaryotic vectors. Chatterjee; Saswati, et al. 435/320.1; 424/93.1 424/93.2. C12N015/86 C12N015/35 C12N005/10

A61K048/00.

39. 5198346. 26 Jul 90; 30 Mar 93. Generation and selection of novel DNA-binding proteins and polypeptides. Ladner; Robert C., et al. 435/69.1; 435/252.3 435/320.1 435/489. C12N015/63 C12N015/09 C12P021/00.

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Terms	Documents
cell$ near10 (E1a or E1b) near5 (regulat$ or induci$) near5 promoter$	39

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Search Results - Record(s) 1 through 22 of 22 returned.

1. 20050003545. 03 Jul 03. 06 Jan 05. Adenovirus packaging cell lines. Li, Yuanhao, et al. 435/456; 435/325 435/366 C12N005/08 C12N015/861.

2. 20050003506. 28 May 04. 06 Jan 05. Adenoviral E1A/E1B complementing cell line. Li, Yuanhao, et al. 435/235.1; 435/366 C12N007/00 C12N005/08.

3. 20040214162. 18 Jul 03. 28 Oct 04. PAV regions for encapsidation and E1 transcriptional control. Tikoo, Suresh K.. 435/5; 536/23.72 C12Q001/70 C07H021/04.

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5. 20040047836. 29 Sep 03. 11 Mar 04. Anti-neoplastic viral agents. Iggo, Richard, et al. 424/93.2; 435/235.1 435/320.1 435/456 A61K048/00 C12N015/86 C12N007/00.

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7. 20030171336. 04 Jun 02. 11 Sep 03. Complementing cell lines. Vogels, Ronald, et al. 514/100; 435/235.1 435/320.1 435/325 514/44 A61K031/70 A01N043/04 A61K031/665 A01N057/00 C12N007/00 C12N007/01 C12N015/00 C12N015/09 C12N015/63 C12N015/70 C12N015/74 C12N005/00 C12N005/02.

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12. 20020168349. 30 Jul 01. 14 Nov 02. Anti-neoplastic viral agents. Iggo, Richard, et al. 424/93.21; 424/93.6 435/235.1 536/23.72 A61K048/00 C12N007/00 C07H021/04 A01N063/00 C12N007/01.

13. 20020019050. 05 Apr 01. 14 Feb 02. Compositions and methods for helper-free production of

recombinant adeno-associated viruses. Gao, Guangping, et al. 435/456; 435/235.1 C12N015/861 C12N007/01.

☐ 14. 6764674. 27 Dec 99; 20 Jul 04. Adenovirus E1B shuttle vectors. Hermiston; Terry, et al. 424/93.2; 435/235.1 435/320.1 435/325 435/358 435/365 435/367 435/455 435/456 435/471. A01N063/00 A61K048/00.

☐ 15. 6692736. 21 Mar 01; 17 Feb 04. Cell-specific adenovirus vectors comprising an internal ribosome entry site. Yu; De-Chao, et al. 424/93.2; 435/235.1 435/320.1 435/369 435/375 435/457 435/69.1 435/91.4 435/91.41 435/91.42 514/44. C12P021/06 C12P007/00 C12P015/00 C12N005/10 C12N007/02 C12N015/86.

☐ 16. 6544507. 30 Jul 01; 08 Apr 03. Anti-neoplastic viral agents. Iggo; Richard, et al. 424/93.2; 435/235.1 435/320.1 435/471 435/475 435/91.33 435/91.4 514/44. A61K048/00 A61K035/76 C12N007/01 C12N015/861.

☐ 17. 6492169. 15 Nov 00; 10 Dec 02. Complementing cell lines. Vogels; Ronald, et al. 435/325; 435/235.1 435/455 435/69.1. C12N005/02 C12N007/00 C12N015/63.

☐ 18. 6485966. 05 Apr 01; 26 Nov 02. Compositions and methods for helper-free production of recombinant adeno-associated viruses. Gao; Guangping, et al. 435/320.1; 435/235.1 435/239 435/325 435/455 435/466 514/44 536/23.1. C12N015/861 C12N007/01 C12N015/09 A61K048/00 C07H021/04.

☐ 19. 6258595. 23 Sep 99; 10 Jul 01. Compositions and methods for helper-free production of recombinant adeno-associated viruses. Gao; Guang-Ping, et al. 435/320.1; 435/239 435/325 435/455 435/466 514/44 536/23.1. C12N015/86 C12N015/00 C12N005/00 C07H021/04 A61K048/00.

☐ 20. 6228646. 07 Mar 97; 08 May 01. Helper-free, totally defective adenovirus for gene therapy. Hardy; Stephen F.. 435/455; 435/320.1 435/456 435/457. C12N015/00.

☐ 21. US20050003545A. New adenovirus packaging cell line permissive for replication of an E1A/E1B deficient adenovirus vector, useful for producing recombinant adenoviral vectors, e.g. replication competent adenoviral vectors, or oncolytic adenoviral vectors. FARSON, D, et al. C12N000/00 C12N005/08 C12N015/861.

☐ 22. US 6764674B. New recombinant adenoviral vector comprises a deletion in the E1b region, useful for gene therapy, e.g. treating or preventing diseases including neoplastic conditions. HERMISTON, T, et al. A01N063/00 A61K048/00.

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Terms	Documents
(E1b or E1b) near5 ("same" or identical or different or heterologous) near5 promoter$	22

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Day : Friday
Date: 3/11/2005

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Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.
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      Set  Items  Description
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? set hi ;set hi
HILIGHT set on as ''
HILIGHT set on as ''
? begin 5,6,55,154,156,312,399,biotech,biosci
>>>         135 is unauthorized
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      Set  Items  Description
      ---  -----  -----------
? s (E1a or E1b) (5n) ("same" or identical) (5n) promoter?
           31821  E1A
            7673  E1B
         4857368  SAME
         1074462  IDENTICAL
         1082542  PROMOTER?
      S1      97  (E1A OR E1B) (5N) ("SAME" OR IDENTICAL) (5N) PROMOTER?
? s s1 and (A549 or PC-3)
              97  S1
           30149  A549
             473  PC-3
      S2       9  S1 AND (A549 OR PC-3)
? rd s2
>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S3       2  RD S2 (unique items)
? d s3/9/1-2
      Display 3/9/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.

0013813287   BIOSIS NO.: 200200406798
Transcriptional targeting of conditionally replicating adenovirus to
  dividing endothelial cells
AUTHOR: Savontaus M J; Sauter B V; Huang T-G; Woo S L C (Reprint)
AUTHOR ADDRESS: Mount Sinai School of Medicine, Institute for Gene Therapy
  and Molecular Medicine, 1425 Madison Avenue, Box 1496, New York, NY,
  10029, USA**USA
JOURNAL: Gene Therapy  9 (14): p972-979 July, 2002 2002
MEDIUM: print
ISSN: 0969-7128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Conditionally replicating adenoviruses (CRADs) are a novel
  strategy in cancer treatment and clinical trials using CRADs targeted to

                                    -more-
?
      Display 3/9/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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  tumor cells have been reported recently. We hypothesized that it would be
  possible to construct CRADs targeted to dividing endothelial cells, which
  are present in the tumor endothelium. We utilized the regulatory elements
  of Flk-1 and endoglin genes, which have been shown to be highly
  overexpressed in angiogenic endothelial cells, to construct two CRADs:
  Ad.Flk-1, which has adenoviral E1A gene under the control of the Flk-1
  enhancer/promoter, and Ad.Flk-Endo, which harbors the   ***same***   Flk-1
  enhancer/  ***promoter***   as Ad.Flk-1, plus it has the adenoviral   ***E1B***
  gene under control of the endoglin   ***promoter***   . Viral titer
  measurements by plaque assay showed that in human umbilical vein
  endothelial cells (HUVECs), both CRADs replicated at levels comparable to
  that of wild-type adenovirus. In Flk-1 and endoglin negative Hep3B and
    ***A549***   cells, however, the replication of Ad.Flk-1 and Ad.Flk-Endo
  was reduced by 30-fold and 600-fold, respectively. Cytotoxicity assays
  demonstrated that both CRADs killed HUVECs as effectively as wild-type
  adenovirus and their cytotoxicity in Hep3B and A549 cells was
  comparable to nonreplicating control adenovirus. Furthermore, there was a

                                    -more-
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Display 3/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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striking inhibition (83-91%) of capillary network formation in an in vitro angiogenesis assay when HUVECs were infected with Ad.Flk-1 or Ad.Flk-Endo as compared with the nonreplicating control virus. These results demonstrate that CRADs can be transcriptionally targeted to dividing endothelial cells with high specificity, and that the combined use of Flk-1 and endoglin regulatory elements has a synergistic effect on targeting specificity. This principle may be incorporated into novel therapeutic agents to develop anti-angiogenic treatment for cancer.

DESCRIPTORS:
MAJOR CONCEPTS: Cell Biology; Molecular Genetics--Biochemistry and Molecular Biophysics; Tumor Biology
BIOSYSTEMATIC NAMES: Adenoviridae--dsDNA Viruses, Viruses, Microorganisms ; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: adenovirus (Adenoviridae)--conditionally replicating; **A549** cell line (Hominidae); HUVEC cell line (Hominidae)--human umbilical vein endothelial cells; Hep3B cell line (Hominidae

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Display 3/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.
ORGANISMS: PARTS ETC: endothelial cell--circulatory system
COMMON TAXONOMIC TERMS: Double-Stranded DNA Viruses; Microorganisms; Viruses; Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: cancer--neoplastic disease, drug therapy
MESH TERMS: Neoplasms (MeSH)
GENE NAME: human Flk-1 gene (Hominidae); human endoglin gene (Hominidae)
MISCELLANEOUS TERMS: angiogenesis; cell division; transcriptional targeting
CONCEPT CODES:
02502 Cytology - General
02506 Cytology - Animal
02508 Cytology - Human
03502 Genetics - General
03508 Genetics - Human
14504 Cardiovascular system - Physiology and biochemistry
24004 Neoplasms - Pathology, clinical aspects and systemic effects
31500 Genetics of bacteria and viruses

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Display 3/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.
33506 Virology - Animal host viruses
BIOSYSTEMATIC CODES:
03116 Adenoviridae
86215 Hominidae

- end of record -
?
Display 3/9/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.

0358737 DBR Accession Number: 2005-04441 PATENT
New adenovirus packaging cell line permissive for replication of an E1A/E1B deficient adenovirus vector, useful for producing recombinant adenoviral vectors, e.g. replication competent adenoviral vectors, or oncolytic adenoviral vectors - packaging cell culture for adeno virus vector construction for use in gene therapy
AUTHOR: LI Y; FARSON D; TAO L; YU D
PATENT ASSIGNEE: LI Y; FARSON D; TAO L; YU D 2005

PATENT NUMBER: US 20050003545 PATENT DATE: 20050106 WPI ACCESSION NO.: 2005-065249 (200507)
PRIORITY APPLIC. NO.: US 613106 APPLIC. DATE: 20030703
NATIONAL APPLIC. NO.: US 613106 APPLIC. DATE: 20030703
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - An adenovirus packaging cell line permissive for replication of an E1A/E1B deficient adenovirus vector comprising a first expression vector and a second expression vector

-more-

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Display 3/9/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.
stably integrated into the genome of the cell line, is new. DETAILED DESCRIPTION - An adenovirus packaging cell line permissive for replication of an E1A/E1B deficient adenovirus vector comprises an adenovirus E1A coding sequence and an adenovirus E1B coding sequence operably linked to a promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B promoter. It comprises a first expression vector and a second expression vector stably integrated into the genome of the cell line, where the first vector comprises adenovirus E1A coding sequences, operatively linked to a non-adenoviral heterologous promoter, and the second vector comprises adenovirus E1B coding sequences operatively linked to a non-adenoviral heterologous promoter. INDEPENDENT CLAIMS are also included for: (1) producing an adenovirus packaging cell line permissive for replication of an EIA/E1B deficient adenovirus vector; and (2) producing E1A/E1B deficient adenovirus. BIOTECHNOLOGY - Preferred Cell Line: The adenovirus E1A coding sequence and the adenovirus E1B coding sequence are stably integrated into mid cell line, operably linked to identical promoters,

-more-

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Display 3/9/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.
operably linked to the same promoter, operably linked to different promoters, or stably integrated at different sites in the cell line. Preferably, the cell line is a human cell line selected from **A549** cells permissive for adenovirus replication PC-3 cells or primary cells permissive for adenovirus production. The promoter that lacks substantial sequence identity with a native adenovirus E1A or EIB promoter is a constitutive promoter and/or a regulatable promoter. Preferably, the promoter is a retrovirus promoter. The adenovirus E1A coding sequence encodes an adenovirus 243 gene product, 289 gene product, or both 243 and 289 gene product. The adenovirus E1A coding sequence comprises 986 bp (SEQ ID NO. 1). The adenovirus E1B coding sequence encodes adenovirus 19 Kd gene product, 55 Kd gene product, or both 19 and 55 Kd gene product. The adenovirus E1B coding sequence comprises 2144 bp (SEQ ID NO. 4). Preferred Method: Producing an adenovirus packaging cell line permissive for replication of an E1A/E1B deficient adenovirus vector comprises introducing into a cell line permissive for adenovirus replication, an expression vector comprising:

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Display 3/9/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.
(a) an adenovirus EIA coding sequence operably linked to a promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B promoter; and (b) an adenovirus E1B coding sequence operably linked to a promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B ***promoter*** . The adenovirus E1A coding sequence and the adenovirus **E1B** coding sequence are present on separate and/or ***same*** vectors. The ***E1A*** and ***E1B*** expression vectors are both retroviral expression vectors. Producing

E1A/E1B deficient adenovirus comprises introducing an E1A/E1B deficient adenovirus into the packaging cell line, and recovering from the cell line a population of adenovirus substantially free of replication competent adenovirus. USE - The adenovirus packaging cell line is useful for producing recombinant adenoviral vectors, e.g. replication competent adenoviral vectors, oncolytic adenoviral vectors, or replication defective adenoviral vectors. It is particularly useful for producing stocks of adenoviral particles with minimal potential for recombination events between the packaging cell line genome and the

-more-

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Display 3/9/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.
adenoviral vector. It can also be used for clinical applications. ADMINISTRATION - Administration can be through oral, nasal, buccal, rectal, vaginal, topical, orthotopic, intradermal, subcutaneous, intramuscular, intraperitoneal, or intravenous routes. No dosage details given. EXAMPLE - Naive ***A549*** cells (ATCC Number CCl-185) were cultured in complete medium including DME/High, 10% fetal bovine serum, 1% glutamine and 1% Pen-Strep. Adenoviral E1A and E1B coding sequences were stably introduced into **A549** cells by co-infecting the cells with MMLV-E1A and MMLV-E1B viruses by spinoculation. 1x105 cells were resuspended in 1 ml of E1A/E1B viral supernatants and 8 microl/ml of polybrene. The cell and virus mixture was then centrifuged at 3400 rpm at 34 degrees Centigrade for 4 hours. After spinoculation, the populations were resuspended with complete medium, transferred into 6-well plates and incubated in 5% incubator at 37 degrees Centigrade for 8 days. The populations were dilution cloned on 10-cm dishes. Clones were picked into 96-well plates, and duplicate wells were made. These were grown for 5 days to allow cell expansion. (23 pages)

-more-

?
Display 3/9/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.
DESCRIPTORS: replication competent, oncolytic, replication defective adeno virus vector construction, **A549** cell, packaging cell culture, E1A, E1B promoter, appl. gene therapy (24, 07)
SECTION: THERAPEUTICS-Gene Therapy-GENETIC TECHNIQUES and APPLICATIONS-Gene Expression Techniques and Analysis; BIOMANUFACTURING and BIOCATALYSIS-Animal/Plant Cell Culture

- end of record -

?
? rd s1
>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.
Display 3/9/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.
...examined 50 records (50)
...completed examining records
S4 28 RD S1 (unique items)
? d s4/3/1-28
Display 4/3/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.

0015180650 BIOSIS NO.: 200500087715
Repression of the melanocyte-specific promoter of the microphthalmia-associated transcription factor by the adenoviral E1A 12S oncoprotein
AUTHOR: Drdova B; Vachtenheim J (Reprint)
AUTHOR ADDRESS: Mol Biol LabUniv HospClin Pneumol,Med Fac 3, Charles Univ,

Budinova 2, CR-18000, Prague, 8, Czech Republic**Czech Republic
AUTHOR E-MAIL ADDRESS: jivach@upn.anet.cz
JOURNAL: Folia Biologica (Prague) 50 (5): p159-166 2004 2004
MEDIUM: print
ISSN: 0015-5500
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

- end of record -

?
Display 4/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013895791 BIOSIS NO.: 200200489302
Transcriptional deregulation of the keratin 18 gene in human colon carcinoma cells results from an altered acetylation mechanism
AUTHOR: Prochasson Philippe; Delouis Cecile; Brison Olivier (Reprint)
AUTHOR ADDRESS: Laboratoire de Genetique Oncologique, UMR 1599 CNRS, Institut Gustave-Roussy, 39 rue Camille Desmoulins, 94805, Villejuif Cedex, France**France
JOURNAL: Nucleic Acids Research 30 (15): p3312-3322 August 1, 2002 2002
MEDIUM: print
ISSN: 0305-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

- end of record -

?
Display 4/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013813287 BIOSIS NO.: 200200406798
Transcriptional targeting of conditionally replicating adenovirus to dividing endothelial cells
AUTHOR: Savontaus M J; Sauter B V; Huang T-G; Woo S L C (Reprint)
AUTHOR ADDRESS: Mount Sinai School of Medicine, Institute for Gene Therapy and Molecular Medicine, 1425 Madison Avenue, Box 1496, New York, NY, 10029, USA**USA
JOURNAL: Gene Therapy 9 (14): p972-979 July, 2002 2002
MEDIUM: print
ISSN: 0969-7128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

- end of record -

?
Display 4/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012357238 BIOSIS NO.: 200000075551
Properties of the adenovirus type 40 E1B promoter that contribute to its low transcriptional activity
AUTHOR: Mautner Vivien (Reprint); Bailey Andy; Steinthorsdottir Valgerdur; Ullah Robina; Rinaldi Angela
AUTHOR ADDRESS: CRC Institute for Cancer Studies, University of Birmingham, Edgbaston, Birmingham, B15 2TA, UK**UK
JOURNAL: Virology 265 (1): p10-19 Dec. 5, 1999 1999
MEDIUM: print
ISSN: 0042-6822
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

```
                                - end of record -
? s s4 and packaging (n) cell?
Processing
Processing
Processed  10 of  35 files ...
Processing
Processing
Processed  20 of  35 files ...
Completed processing all files
              28  S4
          296283  PACKAGING
        23178353  CELL?
            7833  PACKAGING(N)CELL?
      S5       1  S4 AND PACKAGING (N) CELL?
? d s5/3/1
      Display 5/3/1     (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.

0358737  DBR Accession No.: 2005-04441    PATENT
New adenovirus packaging cell line permissive for replication
    of an E1A/E1B deficient adenovirus vector, useful for producing
    recombinant adenoviral vectors, e.g. replication competent adenoviral
    vectors, or oncolytic adenoviral vectors - packaging cell
    culture for adeno virus vector construction for use in gene therapy
AUTHOR: LI Y;  FARSON D;  TAO L;  YU D
PATENT ASSIGNEE: LI Y;  FARSON D;  TAO L;  YU D  2005
PATENT NUMBER: US 20050003545  PATENT DATE: 20050106  WPI ACCESSION NO.:
    2005-065249  (200507)
PRIORITY APPLIC. NO.: US 613106  APPLIC. DATE: 20030703
NATIONAL APPLIC. NO.: US 613106  APPLIC. DATE: 20030703
LANGUAGE: English

                                - end of record -
? s (E1a or E1b) (5n) ("same" or identical or different or heterologous) (5n) promoter?
Processed  20 of  35 files ...
Processing
Completed processing all files
           31821  E1A
            7673  E1B
         4857368  SAME
         1074462  IDENTICAL
        10069300  DIFFERENT
          247734  HETEROLOGOUS
         1082542  PROMOTER?
      S6     313  (E1A OR E1B) (5N) ("SAME" OR IDENTICAL OR DIFFERENT OR
                  HETEROLOGOUS) (5N) PROMOTER?
? rd s6
>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...examined 50 records  (300)
...completed examining records
      S7      89  RD S6 (unique items)
? s s7 and (A549 or PC-3)
              89  S7
           30149  A549
             473  PC-3
      S8       3  S7 AND (A549 OR PC-3)
? s s7 and packaging (n) cell?
Processing
Processed  10 of  35 files ...
```

Processing
Processing
Processed 20 of 35 files ...
Completed processing all files
89 S7
296283 PACKAGING
23178353 CELL?
7833 PACKAGING(N)CELL?
S9 3 S7 AND PACKAGING (N) CELL?
? d s9/3/1-3
Display 9/3/1 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.

0358737 DBR Accession No.: 2005-04441 PATENT
New adenovirus **packaging cell** line permissive for replication of an E1A/E1B deficient adenovirus vector, useful for producing recombinant adenoviral vectors, e.g. replication competent adenoviral vectors, or oncolytic adenoviral vectors - **packaging cell** culture for adeno virus vector construction for use in gene therapy
AUTHOR: LI Y; FARSON D; TAO L; YU D
PATENT ASSIGNEE: LI Y; FARSON D; TAO L; YU D 2005
PATENT NUMBER: US 20050003545 PATENT DATE: 20050106 WPI ACCESSION NO.: 2005-065249 (200507)
PRIORITY APPLIC. NO.: US 613106 APPLIC. DATE: 20030703
NATIONAL APPLIC. NO.: US 613106 APPLIC. DATE: 20030703
LANGUAGE: English

- end of record -
?
Display 9/3/2 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2005 Thomson Derwent & ISI. All rts. reserv.

0297272 DBR Accession No.: 2002-19119 PATENT
Novel **packaging cell** line capable of complementing recombinant adenovirus based on serotype from subgroup B, useful for producing human recombinant therapeutic proteins such as human growth factors and antibodies - HEK-293 **cell packaging cell** culture for adeno virus vector construction for use in gene therapy
AUTHOR: VOGELS R; HAVENGA M J E; MEHTALI M
PATENT ASSIGNEE: CRUCELL HOLLAND BV 2002
PATENT NUMBER: WO 200240665 PATENT DATE: 20020523 WPI ACCESSION NO.: 2002-519382 (200255)
PRIORITY APPLIC. NO.: US 713678 APPLIC. DATE: 20001115
NATIONAL APPLIC. NO.: WO 2001NL824 APPLIC. DATE: 20011114
LANGUAGE: English

- end of record -
?
Display 9/3/3 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0293994 DBR Accession No.: 2002-15841 PATENT
Vector system for preparing recombinant adeno-associated viral particles, used for high-level expression of heterologous therapeutic proteins in eukaryotic cells - vector-mediated gene transfer, expression in host cell and **packaging cell** culture for gene therapy
AUTHOR: ORBERGER G; HELLMUTH K; WAGENER C
PATENT ASSIGNEE: ARIMEDES BIOTECHNOLOGY GMBH 2002
PATENT NUMBER: WO 200238782 PATENT DATE: 20020516 WPI ACCESSION NO.: 2002-435853 (200246)
PRIORITY APPLIC. NO.: DE 1056210 APPLIC. DATE: 20001113
NATIONAL APPLIC. NO.: WO 2001EP13125 APPLIC. DATE: 20011113
LANGUAGE: German

- end of record -

? d s9/9/1-3
Display 9/9/1 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0358737 DBR Accession No.: 2005-04441 PATENT
New adenovirus **packaging cell** line permissive for replication of an E1A/E1B deficient adenovirus vector, useful for producing recombinant adenoviral vectors, e.g. replication competent adenoviral vectors, or oncolytic adenoviral vectors - **packaging cell** culture for adeno virus vector construction for use in gene therapy
AUTHOR: LI Y; FARSON D; TAO L; YU D
PATENT ASSIGNEE: LI Y; FARSON D; TAO L; YU D 2005
PATENT NUMBER: US 20050003545 PATENT DATE: 20050106 WPI ACCESSION NO.: 2005-065249 (200507)
PRIORITY APPLIC. NO.: US 613106 APPLIC. DATE: 20030703
NATIONAL APPLIC. NO.: US 613106 APPLIC. DATE: 20030703
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - An adenovirus **packaging cell** line permissive for replication of an E1A/E1B deficient adenovirus vector comprising a first expression vector and a second

-more-
?
Display 9/9/1 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

expression vector stably integrated into the genome of the cell line, is new. DETAILED DESCRIPTION - An adenovirus ***packaging*** ***cell*** line permissive for replication of an E1A/E1B deficient adenovirus vector comprises an adenovirus E1A coding sequence and an adenovirus E1B coding sequence operably linked to a promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B promoter. It comprises a first expression vector and a second expression vector stably integrated into the genome of the cell line, where the first vector comprises adenovirus **E1A** coding sequences, operatively linked to a non-adenoviral **heterologous promoter**, and the second vector comprises adenovirus **E1B** coding sequences operatively linked to a non-adenoviral ***heterologous*** ***promoter*** . INDEPENDENT CLAIMS are also included for: (1) producing an adenovirus **packaging cell** line permissive for replication of an EIA/E1B deficient adenovirus vector; and (2) producing E1A/E1B deficient adenovirus. BIOTECHNOLOGY - Preferred Cell Line: The adenovirus E1A coding sequence and the

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Display 9/9/1 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

adenovirus E1B coding sequence are stably integrated into mid cell line, operably linked to identical promoters, operably linked to the same promoter, operably linked to different promoters, or stably integrated at different sites in the cell line. Preferably, the cell line is a human cell line selected from A549 cells permissive for adenovirus replication PC-3 cells or primary cells permissive for adenovirus production. The promoter that lacks substantial sequence identity with a native adenovirus E1A or EIB promoter is a constitutive promoter and/or a regulatable promoter. Preferably, the promoter is a retrovirus promoter. The adenovirus E1A coding sequence encodes an adenovirus 243 gene product, 289 gene product, or both 243 and 289 gene product. The adenovirus E1A coding sequence comprises 986 bp (SEQ ID NO. 1). The adenovirus E1B coding sequence encodes adenovirus 19 Kd gene product, 55 Kd gene product, or both 19 and 55 Kd gene product. The adenovirus E1B coding sequence comprises 2144 bp (SEQ ID NO. 4). Preferred Method: Producing an adenovirus **packaging cell** line permissive for replication of an E1A/E1B deficient adenovirus

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Display 9/9/1 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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vector comprises introducing into a cell line permissive for adenovirus replication, an expression vector comprising: (a) an adenovirus E1A coding sequence operably linked to a **promoter** that lacks substantial sequence identity with a native adenovirus **E1A** or **E1B promoter**; and (b) an adenovirus **E1B** coding sequence operably linked to a **promoter** that lacks substantial sequence identity with a native adenovirus **E1A** or **E1B** ***promoter*** . The adenovirus ***E1A*** coding sequence and the adenovirus **E1B** coding sequence are present on separate and/or ***same*** vectors. The E1A and E1B expression vectors are both retroviral expression vectors. Producing E1A/E1B deficient adenovirus comprises introducing an E1A/E1B deficient adenovirus into the **packaging cell** line, and recovering from the cell line a population of adenovirus substantially free of replication competent adenovirus. USE - The adenovirus ***packaging*** ***cell*** line is useful for producing recombinant adenoviral vectors, e.g. replication competent adenoviral vectors, oncolytic adenoviral vectors, or

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Display 9/9/1 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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replication defective adenoviral vectors. It is particularly useful for producing stocks of adenoviral particles with minimal potential for recombination events between the **packaging cell** line genome and the adenoviral vector. It can also be used for clinical applications. ADMINISTRATION - Administration can be through oral, nasal, buccal, rectal, vaginal, topical, orthotopic, intradermal, subcutaneous, intramuscular, intraperitoneal, or intravenous routes. No dosage details given. EXAMPLE - Naive A549 cells (ATCC Number CCl-185) were cultured in complete medium including DME/High, 10% fetal bovine serum, 1% glutamine and 1% Pen-Strep. Adenoviral E1A and E1B coding sequences were stably introduced into A549 cells by co-infecting the cells with MMLV-E1A and MMLV-E1B viruses by spinoculation. 1x105 cells were resuspended in 1 ml of E1A/E1B viral supernatants and 8 microl/ml of polybrene. The cell and virus mixture was then centrifuged at 3400 rpm at 34 degrees Centigrade for 4 hours. After spinoculation, the populations were resuspended with complete medium, transferred into 6-well plates and incubated in 5% incubator at 37 degrees Centigrade

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Display 9/9/1 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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for 8 days. The populations were dilution cloned on 10-cm dishes. Clones were picked into 96-well plates, and duplicate wells were made. These were grown for 5 days to allow cell expansion. (23 pages)
DESCRIPTORS: replication competent, oncolytic, replication defective adeno virus vector construction, A549 **cell**, **packaging cell** culture, E1A, E1B promoter, appl. gene therapy (24, 07)
SECTION: THERAPEUTICS-Gene Therapy-GENETIC TECHNIQUES and APPLICATIONS-Gene Expression Techniques and Analysis; BIOMANUFACTURING and BIOCATALYSIS-Animal/Plant Cell Culture

- end of record -

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Display 9/9/2 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0297272 DBR Accession Number: 2002-19119 PATENT

Novel **packaging cell** line capable of complementing recombinant adenovirus based on serotype from subgroup B, useful for producing human recombinant therapeutic proteins such as human growth factors and antibodies - HEK-293 **cell packaging cell** culture for adeno virus vector construction for use in gene therapy
AUTHOR: VOGELS R; HAVENGA M J E; MEHTALI M
PATENT ASSIGNEE: CRUCELL HOLLAND BV 2002
PATENT NUMBER: WO 200240665 PATENT DATE: 20020523 WPI ACCESSION NO.: 2002-519382 (200255)
PRIORITY APPLIC. NO.: US 713678 APPLIC. DATE: 20001115
NATIONAL APPLIC. NO.: WO 2001NL824 APPLIC. DATE: 20011114
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A **packaging cell** line (I) capable of complementing recombinant adenovirus based on a serotype from subgroup B, is new. DETAILED DESCRIPTION - An INDEPENDENT CLAIM is

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also included for a recombinant adenovirus (II) produced using (I). BIOTECHNOLOGY - Preferred Cell Line: In (I), the serotype from subgroup B is adenovirus type 35. (I) is derived from primary, diploid human cells, or its derivatives, where the primary, diploid human cells, or its derivatives, have been transformed by adenovirus E1 coding sequences either operatively linked on one DNA molecule or located on two separate DNA molecules, where the adenovirus E1 coding sequences are operatively linked to regulatory sequences enabling transcription and translation of encoded proteins. The primary, diploid human cells, or its derivatives, are selected from primary human retinoblasts, primary human embryonic kidney cells, and primary human amniocytes. The primary, diploid human cells, or its derivatives, have been transfected with an adenovirus E1A coding sequence to induce unlimited proliferation. (I) further comprises an E1B coding sequence. The primary, diploid human cells, or its derivatives, have been transformed by expression of adenovirus E1 proteins of a subgroup other than subgroup C, where the subgroup other than subgroup C is subgroup B. The

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adenovirus E1 proteins are derived from adenovirus type 35. The primary, diploid human cells, or its derivatives, have been transformed with a chimeric adenovirus E1 construct comprising part of a first adenovirus E1 coding sequence of a first adenovirus serotype that enables efficient transformation of primary human cells or its derivatives, and part of a second adenovirus E1 coding sequence of a second adenovirus serotype, where the second adenovirus E1 coding sequence provides the serotype-specific adenovirus E1B functions that enable efficient propagation of recombinant adenovirus E1-deleted viruses of the second adenovirus serotype. The first adenovirus serotype is a subgroup C adenovirus and the second adenovirus serotype is a subgroup B adenovirus, preferably adenovirus type 35. The E1A coding sequence and at least part of the E1B-21K coding sequence are derived from a subgroup C adenovirus, and the E1B-55K coding sequence as far as not overlapping with the 21K coding sequence is derived from a subgroup B adenovirus. All E1 coding sequences are derived from a subgroup C adenovirus, except for at least a part of the E1B-55K coding

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sequence that is necessary for serotype-specific complementation of an

alternative adenovirus serotype, where the E1B coding sequence is derived from the alternative adenovirus serotype. (I) comprises bovine adenovirus E1B-55K. The complementing recombinant adenovirus is derived from a bovine adenovirus. The primary, diploid human cells, or its derivatives, have been transformed by adenovirus E1 coding sequences located on two separate DNA molecules, where the first DNA molecule carries at least part of the E1 coding sequences of the serotype enabling efficient transformation and the second DNA molecule carries at least part of the sequences necessary for serotype-specific complementation. The derivative cells are PER.C6 (ECACC deposit number 96022940) which further comprise an Ad35-E1 region integrated into their genome, and the Ad35-E1 region is present in a functional expression cassette. The Ad35-E1 region does not contain sequences overlapping with sequences present in an associated recombinant viral vector. The functional expression cassette comprises a heterologous promoter and a poly-adenylation signal functionally linked to the

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Ad35-E1 region, where the heterologous promoter is a human phosphoglycerate gene promoter (hPGK) and the poly-adenylation signal is a hepatitis B virus poly-adenylation signal (HBV-pA). The Ad35-E1 region comprises the coding regions of the E1A proteins and the E1B promoter sequence linked to E1B coding sequences up to and including the stop codon of the E1B 55K protein. The Ad35-E1 region comprises nucleotides 468 to and including nucleotide 3400 of the Ad35 wild-type. (I) is derived from PER.C6 (ECACC deposit number 96022940), and comprises Ad35-E1B coding sequences. The Ad35- ***E1B*** coding sequences are driven by an **E1B promoter**, a hPGK **promoter** or an elongation factor-1alpha (EF-1alpha) **promoter** and terminated by a **heterologous** poly-adenylation signal such as a hepatitis B virus poly-adenylation signal (HBV-pA). The Ad35-E1B coding sequences comprise the coding sequences of the E1B 21K and the E1B 55K proteins located between nucleotides 1611 and 3400 of the wild-type Ad35 sequence. The Ad35-E1B coding sequences comprise nucleotides 1550 to and including nucleotide 3400 of the wild-type Ad35

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sequence. The Ad35-E1B coding sequences comprise the coding sequences of the E1B-55K gene located between 1916 and 3400 of the wild type Ad35 sequence. (I) lacks a functional coding sequence for E1B-21K. (I) further comprises a DNA encoding at least E4-orf6 of an adenovirus of subgroup B. Preferred Adenovirus: (II) comprises a deletion of nucleic acid encoding at least one E1-region protein or E3-region protein and/or at least one E4-region protein. ACTIVITY - None given. MECHANISM OF ACTION - Gene therapy. No biological data is given. USE - (I) is useful for complementing a recombinant adenovirus by providing (I) with the recombinant adenovirus, culturing the cell to allow for complementation, and harvesting complemented recombinant adenovirus, where the recombinant adenovirus is derived from (adenovirus) a subgroup B adenovirus or adenovirus type 35. (II) is useful for the preparation of a medicament. (All claimed). (I) is useful for producing human recombinant therapeutic proteins such as human growth factors and human antibodies, and for producing human viruses other than adenovirus such as influenza virus, herpes simplex virus, rotavirus, or measles

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virus. (II) is useful for gene therapy and vaccination. EXAMPLE - Generation of cell lines capable of complementing E1-deleted Ad35 viruses was as follows: The construct pIG.E1A.E1B that contained E1 region sequences of Ad5 corresponding to nucleotides 459-3510 of the wildtype Ad5 sequence operatively linked to the human phosphoglycerate kinase promoter (PGK) and the hepatitis B virus polyA sequences was constructed as described in International Patent Application Number W097/00326. The E1 sequences of Ad5 were replaced by corresponding sequences of Ad35. pRSV-Ad35-E1 was digested with EcoRI and Sse83871 and the 3 kbase fragment corresponding to the Ad35 E1 sequences was isolated from gel. Construct pIG.E1A.E1B was digested with Sse8387I completely and partially with EcoRI. The 4.2 kbase fragment corresponding to vector sequences without the Ad5 E1 region but retaining the PGK promoter were separated from other fragments on low melting point (LMP) agarose gel and the correct band was excised from gel. Both obtained fragments were ligated resulting in pIG.Ad35-E1. This vector was further modified to remove the LacZ sequences present

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in the pUC119 vector backbone. The vector was digested with BsaAI and BstXI and the large fragment was isolated from gel. A double stranded oligo was prepared by annealing the following two oligos: 1BB1: 5'-GTGCCTAGGCCACGGGG-3' and 2BB2: 5'-GTGGCCTAGGCAC-3'. Ligation of the oligo and the vector fragment resulted in construct pIG135. Correct insertion of the oligo restored the BsaAI and BstXI sites and introduced a unique AvrII site. Next, a unique site was introduced at the 3' end of the Ad35-E1 expression cassette in pIG135. The construct was digested with SapI and the 3' protruding ends were made blunt by treatment with T4 DNA polymerase. The treated linear plasmid was further digested with BsrGI and the large vector-containing fragment was isolated from gel. To restore the 3' end of the HBV polyA sequence and to introduce a unique site, a polymerase chain reaction (PCR) fragment was generated using the following primers: 3270F: 5'-CACCTCTGCCTAATCATCTC-3' and 4270: GCTCTAGAAATTCCACTGCCTTCCACC-3'. The PCR was performed on pIG.Ad35.E1 DNA using Pwo polymerase. The obtained PCR product was digested with BsrGI and dephosphorylated using

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Tsap enzyme to prevent insert dimerization on the BsrGI site. The PCR fragment and the vector fragment were ligated to yield construct pIG270. New born WAG/RIJ rats were sacrificed at 1 week of gestation and kidneys were isolated. After careful removal of the capsule, kidneys were disintegrated into a single cell suspension. When most of the kidney was trypsinized all cells were re-suspended in Dulbecco's modified eagle medium (DMEM) supplemented with 10 % fetal bovine serum (FBS) and filtered through a sterile cheesecloth. Baby rat kidney (BRK) cells obtained from one kidney were plated in 5 dishes. When a confluency of 70-80 % was reached, the cells were transfected with 1 or 5 micro-g DNA/dish using the CaPO4 precipitation kit. The following constructs were used in separate transfections: pIG.E1A.E1B (expressing the Ad35-E1 region), pRSV.Ad35-E1, pIG.Ad35-E1 and pIG270 (expressing the Ad35-E1 region). Cells were incubated at 37 degrees C, 5 % CO2 until foci of transformed cells appeared. As expected, the Ad5-E1 region efficiently transformed BRK cells. Foci also appeared in the Ad35-E1 transfected cell layer although with lower efficiency. The Ad35

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transformed foci appeared at a later time point: 2 weeks post transfection compared with 7-10 days for Ad5-E1. These experiments clearly showed that the E1 genes of the B group virus Ad35 were capable of transforming primary rodent cells. This proved the functionality of the Ad35-E1 expression constructs and confirmed earlier findings of the transforming capacity of the B-group viruses Ad3 and Ad7. To test if the cells in the foci were really transformed a few foci were picked and expanded. From the 7 picked foci at least 5 turned out to grow as established cell lines.(115 pages)
DESCRIPTORS: cattle subgroup-B, type-35 adeno virus vector construction, primary human retinoblast, HEK-293, human amniocyte, baby rat kidney, **packaging cell** culture, phosphoglycerate-kinase promoter, hepatitis B virus poly-adenylation signal, polymerase chain reaction, DNA primer, appl. gene therapy, human recombinant growth factor, antibody prepare, influenza virus, herpes simplex virus, rota virus, measles virus animal mammal cell culture embryo enzyme EC-2.7.2.3 hepadna virus DNA amplification orthomyxo virus herpes virus reo virus

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paramyxo virus DNA sequence (21, 51)
SECTION: BIOMANUFACTURING and BIOCATALYSIS-Animal/Plant Cell Culture-GENETIC TECHNIQUES and APPLICATIONS-Gene Expression Techniques and Analysis; THERAPEUTICS-Gene Therapy-THERAPEUTICS-Protein Therapeutics; PHARMACEUTICALS-Vaccines

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0293994 DBR Accession Number: 2002-15841 PATENT
Vector system for preparing recombinant adeno-associated viral particles, used for high-level expression of heterologous therapeutic proteins in eukaryotic cells - vector-mediated gene transfer, expression in host cell and **packaging cell** culture for gene therapy
AUTHOR: ORBERGER G; HELLMUTH K; WAGENER C
PATENT ASSIGNEE: ARIMEDES BIOTECHNOLOGY GMBH 2002
PATENT NUMBER: WO 200238782 PATENT DATE: 20020516 WPI ACCESSION NO.: 2002-435853 (200246)
PRIORITY APPLIC. NO.: DE 1056210 APPLIC. DATE: 20001113
NATIONAL APPLIC. NO.: WO 2001EP13125 APPLIC. DATE: 20011113
LANGUAGE: German
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Vector system (A) for preparing recombinant adeno-associated virus (rAAV) particles (VP) comprising: (i) at least two plasmid vectors (PV) that include the two inverted terminal repeats (ITR) of AAV and additional sequences; and (ii)

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plasmid vectors (PV1) without ITRs but containing the rep and cap genes of AAV required for replication and packaging, is new. DETAILED DESCRIPTION - Vector system (A) for preparing recombinant adeno-associated virus (rAAV) particles (VP) comprising: (i) at least two plasmid vectors (PV) that include the two inverted terminal repeats (ITR) of AAV and additional sequences; and (ii) plasmid vectors (PV1) without ITRs but containing the rep and cap genes of AAV required for replication and packaging, is new. The additional sequences in PV are: (a) the E4 gene of adenovirus (AdV), especially the part containing orf6; (b) optionally the E1 gene of AdV, particularly E1B and

specifically the E1B55K-encoding part; (c) optionally one or two heterologous genes X and Y, to be expressed; and (d) optionally the AdV VA and E2A genes. The PV must differ in respect of at least one of (i)-(iii). Components (i)-(iii) are flanked by ITRs so that, after transfection into eukaryotic cells, they are packaged, with the ITRs, into replication-incompetent rAAV virions. INDEPENDENT CLAIMS are also included for: (1) virus stocks containing at least two populations of

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replication-incompetent rAAV virions containing (i)-(iii); (2) preparing recombinant VP by co-transfection into eukaryotic cells; (3) virus stock of rAAV prepared by method (b); (4) expressing a gene in eukaryotic cells using the VP of (b); (5) plasmid kit containing PV in at least two separate compartments or containers; (6) plasmid vector (PV2) containing a fragment of the AdV VA gene, not larger than 0.5 kb, preferably obtained by polymerase chain reaction (PCR) amplification of AdV, especially Ad2, DNA; (7) plasmid vector (PV3) containing components (i) and/or (ii) flanked by ITRs for packaging into replication-incompetent rAAV which contain no coding sequences heterologous to AAV between the ITRs; and (8) plasmid pAdHelp (11492 bp) and plasmid pAIM E1B55K (6575 bp). BIOTECHNOLOGY - Preferred System: Each sequence (i)-(iv) is present in only one PV, and the rep/cap genes may be included in the same PV, but are not flanked by ITRs. The vector containing the rep and cap genes also contains the VA and/or E2A gene. After transfection, the system produces two or three replication incompetent rAAV. Particularly one PV contains the E4 and

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E1B sequences, while the other contains the heterologous gene(s), or one contains the E4 and X components and the other the E1B and Y components, or one contains X while the other contains the E4 and E1B components. In all cases the first PV may also contain the VA and E2A genes. PV are the plasmids described in (h). The E4, ***E1B*** , X and Y genes are controlled by **different heterologous**, preferably inducible, ***promoters*** . Preferred Materials: The VA gene is the fragment described in (f). PV2 may also include the E4 and E1 components, flanked by ITRs, optionally also VA and/or E2A. Typically X and Y encode a heterodimeric glycoprotein, e.g. follicle- or thyroid-stimulating hormones, luteinizing hormone and human chorionic gonadotropin, but also a wide range of non-dimeric proteins such as growth factors, cytokines, urokinase, blood coagulation factors etc., optionally as a fusion protein to facilitate purification. USE - The system is useful for producing rAAV for production of a wide range of therapeutic glycoproteins in eukaryotic cells (claimed). ADVANTAGE - The system provides efficient, large scale production of heterologous

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proteins in mammalian cells, without requiring an adenovirus helper. It is not toxic to host cells and does not cause lysis, so produced proteins are highly pure. EXAMPLE - HEK293 cells were transfected with plasmid pAdHelp (11429 bp, containing the adenoviral E4orf6 sequence between inverted terminal repeats (ITRs) and the E2A gene and minimal VA gene fragment, not flanked by ITRs), the pAIM E1B55K plasmid (6575 bp, containing the adenoviral E1B55K sequence, between ITRs) and the pAAVHelp plasmid (not described, presumably containing rep and cap functions). After 3 days at 37degreesC under 5% carbon dioxide cultured

cells were washed, centrifuged and treated with lytic buffer. After three freeze-thaw cycles, the mixture was centrifuged to recover the clear supernatant as a suspension of recombinant virus particles. These were tested for infectivity in HEK293 cells. (59 pages)
DESCRIPTORS: recombinant adeno-associated virus vector prepare, vector-mediated adeno virus E1, E1B, E1B55K, E2A, FSH, thyrotropin, LH, HCG, somatotropin, cytokine, urokinase, blood coagulation factor, glycoprotein gene transfer, expression in HEK-293 cell, eukaryotic

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packaging ***cell*** culture, polymerase chain reaction, appl. gene therapy parvo virus hormone gonadotropin enzyme protease thrombolytic EC-3.4.21.73 embryo kidney animal human mammal DNA amplification DNA sequence (21, 45)
SECTION: THERAPEUTICS-Gene Therapy-GENETIC TECHNIQUES and APPLICATIONS-Gene Expression Techniques and Analysis; DISEASE-Blood and Hematopoietic Cells-DISEASE-Endocrine/Metabolic System; BIOMANUFACTURING and BIOCATALYSIS-Animal/Plant Cell Culture-DISEASE-Other Diseases

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